

RGH Pharmacy E-Bulletin

Volume 39 (11): October 4, 2010

A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

Editor: Assoc. Prof. Chris Alderman, University of South Australia – Director of Pharmacy, RGH

© Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia 5041

Lithium-induced diabetes insipidus

Lithium remains the gold standard of pharmacological treatment of bipolar disorder. Adverse effects include weight gain, tremor, diarrhoea, polyuria and diabetes insipidus, which can occur in up to 40% of those treated. Drug induced diabetes insipidus is always of the nephrogenic type, thought to be due in part to the lack of response to antidiuretic hormone by aquaporins (water transport channels) in the collecting ducts of the nephrons, which are in turn responsible for the urinary concentrating mechanism. Antidiuretic hormone is thought to open the aquaporins at the cell membrane level via a complex process and this action is inhibited by lithium. Those affected by nephrogenic diabetes insipidus can lose up to 4-6 litre of fluid each day, resulting in increased thirst, polydipsia and possible dehydration.

Diabetes insipidus can be diagnosed by measuring urinary concentrating capacity during a 12 hour water deprivation test, during which urine and serum osmolality and plasma antidiuretic hormone levels are measured before and after administration of desmopressin (or vasopressin). The osmolality results for serum and urine can be used to determine if the patient has complete, partial or no diabetes insipidus at all.

Reversal of lithium induced diabetes insipidus may only require a reduction in the dose of lithium, with treatment augmented with an anticonvulsant such as sodium valproate or carbamazepine. Sometimes, however, lithium may need to be withdrawn altogether and replaced with an anticonvulsant mood stabiliser. If neither of these approaches are feasible or effective, amiloride (5mg twice a day) or hydrochlorthiazide (50mg twice a day) should be tried (strangely, in this context these diuretics produce a paradoxical antidiuretic effect). These agents are thought to prevent lithium from entering aquaporins at the cell membrane level, thereby allowing the action antidiuretic hormone to take effect, reducing polyuria. Indomethacin has also been used, it's mechanism of action thought to be related to sodium and lithium loss, which occur concomitantly. Not all NSAIDs are able to reduce polyuria. It is important to recognise that both NSAIDs and diuretics can significantly increase the serum lithium concentration, which may necessitate a reduction in the lithium maintenance dose if these approaches are used.

Prevention of lithium induced diabetes insipidus involves using the lowest possible dose of lithium and maintaining serum trough levels in the range of 0.4-0.6 mmol/L. Serum trough levels above 1.0 mmol/L should definitely be avoided. A yearly 24-hour measurement of urinary output should be performed as a gradual increase in urinary output may go unnoticed by the patient. Alternative treatment should be considered when urinary volume exceeds 4L/day. Patients should remain adequately hydrated at all times and if at all possible, lithium be administered once a day so the low serum lithium level may allow renal tubular regeneration of cells.

Unfortunately, in a minority of cases, lithium induced nephrogenic diabetes insipidus is not reversible, even with the cessation of lithium therapy: the reason for this is, as of yet, unknown.

This E-Bulletin is based on work by Joanna Hogan, Senior Pharmacist, RGH

FOR FURTHER INFORMATION CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@health.sa.gov.au
Information in this E-Bulletin is derived from critical analysis of available evidence – individual clinical circumstances should be considered when making treatment decisions. You are welcome to forward this E-bulletin by email to others you might feel would be interested, or to print the E-Bulletin for wider distribution. Reproduction of this material is permissible for purposes of individual study or research.

View RGH E-Bulletins at www.auspharmlist.net.au/ebulletin.php